Anthrax
Vaccine
Immunization
Program

Health Care Provider Briefing

Key Messages

- Your health and safety are our #1 concern.
- The threat from anthrax spores is deadly and real.
- America’s best scientists say anthrax vaccine protects against all forms of anthrax disease and is safe.
- Vaccination protects you, your unit, your mission.

History of the Anthrax Vaccine Immunization Program (AVIP)

- Secretary of Defense ordered the AVIP in Dec 97
- Vaccinations began in Southwest Asia in Mar 98 / Vaccinations began in Korea in Aug 98
- Slowdowns in 2000-01. After supply restored, program resumed 2002
- Injunction issued against DoD in Oct 04
- FDA issues Emergency Use Authorization (EUA) in Jan 05
- FDA formally issues Final Rule/Final Order on 19 DEC 05
- AVIP continued as during EUA: same people, voluntary basis
- Deputy Secretary of Defense issued AVIP policy in Oct 06 to re-established a mandatory program for those in higher risk areas and with special roles; policy allows voluntary vaccinations for other groups
- Under Secretary of Defense for Personnel and Readiness released DoD implementation guidance for the AVIP policy in Dec 06

Current Policy Implementation

- **Vaccinations are <u>mandatory</u> for DoD Servicemembers, emergency essential designated civilians, and contractor personnel performing mission-essential services assigned to:**
  - Central Command area of responsibility for 15 or more consecutive days.
  - Korean Peninsula for 15 or more consecutive days
  - Special units with Bio-warfare or Bio-terrorism related missions
  - Specialty units with approved exception to policy

- **Vaccinations shall begin, to the extent feasible, up to 60 days prior to deployment or arrival in higher threat areas.**

Current Policy Implementation

- **Vaccinations are <u>voluntary</u> for DoD Servicemembers:**

  Who are not in the mandatory groups and have received at least one dose of anthrax vaccine absorbed during or after 1998

- **Vaccinations are <u>voluntary</u> for DoD civilians and adult family members; contractors and their accompanying US citizen family members:**

  – Residing in Central Command area of responsibility for 15 or more consecutive days

  - or -

  – Residing on Korean Peninsula for 15 or more consecutive days

- **DoD Civilian Personnel Management Service concluded notification to National Unions 12 Jan 07**

Current Policy Implementation

- Ensure ALL potential vaccine recipients receive the most current educational trifold brochure available, dated 12 Oct 2006 or later.
- Ensure an Individual's Briefing is available at all immunization sites.
- Screen potential vaccine recipients to confirm eligible and not medically exempt.
- Educate potential vaccine recipients about anthrax threat and benefits + risks of vaccination.
- Quality-assurance checklist for clinics posted at www.anthrax.mil

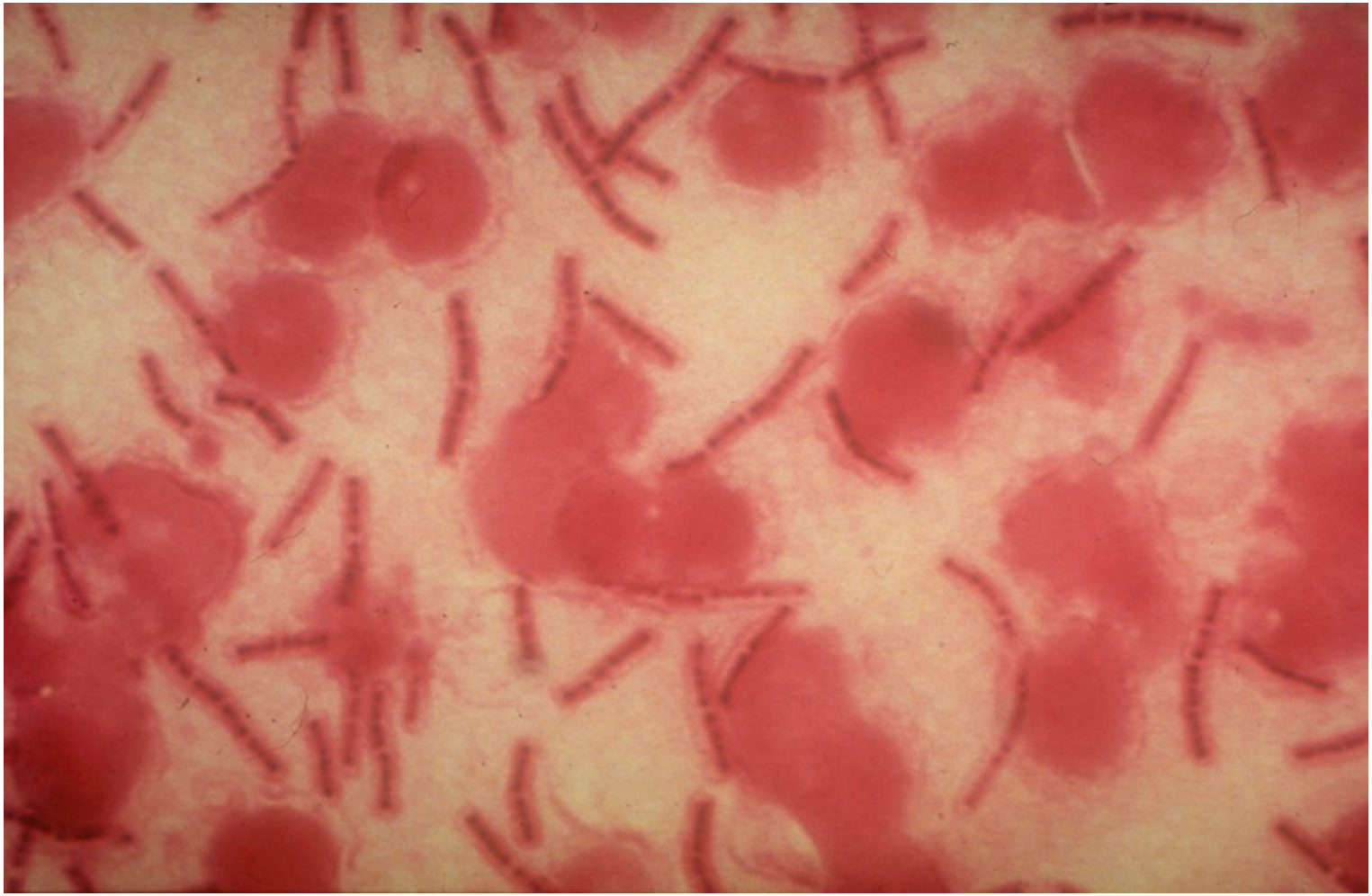
Threat

- Anthrax Spores: the most likely bioweapon.
  - Relatively easy and cheap to produce.
  - Can be stored for a long time.
  - Can be dispersed in air in a variety of ways.
  - Odorless, colorless, tasteless, difficult to detect.
  - Inhalation anthrax is highly lethal.
- Anthrax spores can cause widespread illness and death among unprotected people.

Background: Anthrax Infections

- Recognized as an illness for centuries
- Once common where livestock were raised, now controlled using vaccine for livestock
- Human infection from direct contact with infected animals or animal products or anthrax spores
- Dramatic reduction in U.S. since early 1900s
- Still a problem in Asia and Africa
- Terror attacks via U.S. mail in fall 2001

Microbiology of Anthrax

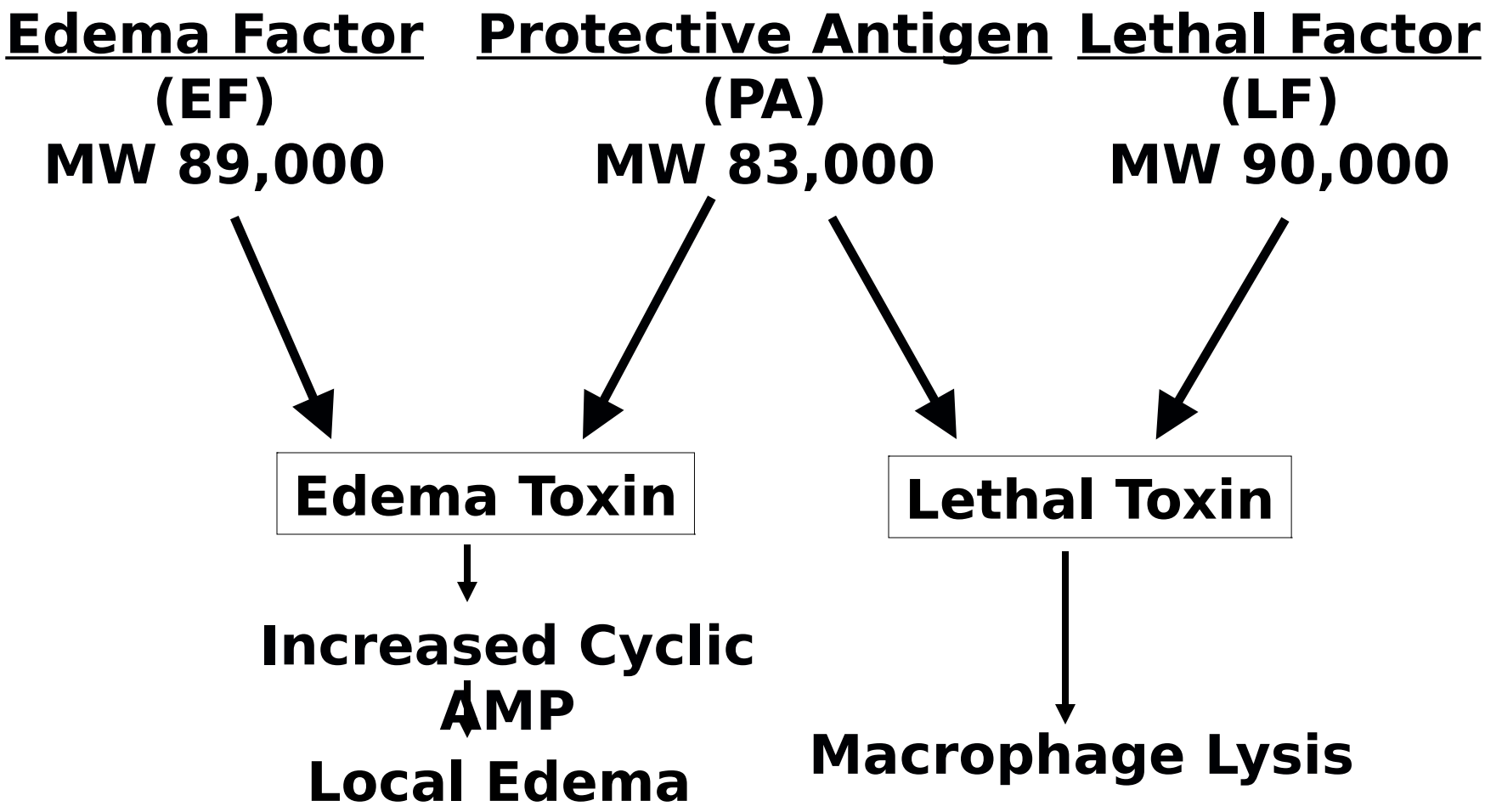


Gram-positive spore-forming rod

Pathogenesis

- Spore enters skin, gastrointestinal tract, or lung
- Ingested by macrophages
- Transported to regional lymph nodes
- Germinate in regional nodes, mediastinum (inhalation)
- Local production of toxins
- Edema & necrosis
- Bacteremia & toxemia
- Seeding of other organ systems

Anthrax Toxins: Building Blocks & Effects



Cutaneous Anthrax

- Greater than 95% of naturally occurring human cases
- Spores enter breaks in skin after contact with contaminated animal products
- Within a few days, a bump (papule) turns into a blister (vesicle), then an ulcer with black area in center (eschar)
- 5% to 20% case-fatality rate, if untreated
- < 1% case-fatality rate, if treated

Gastrointestinal Anthrax

- Ingestion of insufficiently cooked meat from infected animals
- Symptoms include nausea, vomiting, fever and severe abdominal pain
- Lethality rate is ~ 50%, despite treatment

Inhalation Anthrax

- Inhalation anthrax occurs when spores enter the body through the lungs
- Not transmitted from person to person
- Spores migrate to lymph nodes where bacteria multiply and produce lethal toxins
- Toxins cause bleeding and destruction of the brain or vital organs in the chest, resulting in death

Diagnosis of Inhalation Anthrax

- Initial symptoms nonspecific
- Development of respiratory distress
  - Chest X-ray with widened mediastinum
  - Usually no infiltrates
- Sputum not helpful; spores settle in tissue
- Nasal swabs not individually meaningful, www.bt.cdc.gov/DocumentsApp/faqanthrax.asp#Q500
- Blood cultures: positive late in course of illness
- Hemorrhagic pleural effusion or meningitis

Chest X-Ray of Inhalation Anthrax

Inhalation Anthrax Treatment

- Early IV antibiotics and intensive care required
  - Mortality may still reach 50%
  - Penicillin - historical treatment
- Current treatment of choice (2001—multi-antibiotic therapy):
  - Ciprofloxacin 400 mg IV q 8-12 h
  - Doxycycline 200 mg IV x 1, then 100 mg IV q 12 h
- Disease not spread by respiratory secretions
  - Use ‘Standard Precautions’
- Clinical Issues
  - *Emerging Infectious Diseases*, Bioterrorism-Related Anthrax, October 2002 theme issue, www.cdc.gov/ncidod/EID/vol8no10/contents_v8n10.htm

Post-Exposure Prophylaxis

- Starting antibiotics within 24 hours after aerosol exposure should provide significant protection
  - Ciprofloxacin 500 mg po BID (*Cipro*)
  - Doxycyline 100 mg po BID (*Vibramycin*)
  - Levofloxacin 500 mg QD (*Levaquin*)
    - Standard doses are listed; see full prescribing information for more detailed discussion
- For presumptive high-dose exposure, combine antibiotics (acute protection) with vaccination (durable protection)
- Antibiotics are indicated even when fully immunized, to achieve survival as close to 100% as possible

Anthrax Vaccine Facts

- Anthrax vaccine cannot cause anthrax
- Vaccine primes immune system to fight anthrax
- Licensed by the FDA since 1970
  - Administered in U.S. to at-risk veterinarians, laboratory workers, and livestock handlers
  - Over 5.8 million doses to over 1.4 million personnel since Mar 98
- Manufactured in U.S. by Emergent BioSolutions
  - "AVA," *BioThrax*™. Package insert with each vial.
  - Official name: Anthrax vaccine adsorbed, USP
- All doses in schedule needed for full protection
- No other product is approved by FDA to prevent anthrax before exposure

Independent Scientific Reviews

- **FDA Advisory Panel on Bacterial Vaccines and Toxoids** (*Federal Register,* 1985)
- **Defense Health Board** (DHB), advising DoD, 1994 to present
- **Cochrane Collaboration**, Oxford (*Vaccine,* 1998; 2004)
- **Working Group on Civilian Biodefense** (*JAMA,* 1999, 2002)
- CDC's **Advisory Committee on Immunization Practices** (ACIP) (*MMWR,* 2000)
- **Anthrax Vaccine Expert Committee** (AVEC) (*Pharmacoepidemiology & Drug Safety* 2002, 2004)
- **National Academy of Sciences** (IOM), 2002
- **FDA Review of VAERS reports supporting FDA's Final Rule and Final Order** (2005)

Vaccine Quality Control

- Each lot of each vaccine distributed in U.S. must meet FDA specifications before release into interstate commerce:
  - Potency, Sterility, Purity, General Safety
- Manufacturer tests each lot, submits results to FDA
- DoD uses only lots FDA explicitly authorizes for release

Handling Anthrax Vaccine

- Keep anthrax vaccine refrigerated
  - Store between 36° to 46° Fahrenheit (2° to 8° C)
- Do not freeze. Check temperatures daily. Keep log.
- Do not pre-draw vaccine into syringes, unless labeled, refrigerated, and used within the same day.
- Once vial opened, use until expired
- Go to USAMMA web site for guidance on cold-chain management:
  - www.usamma.army.mil/vaccines/anthrax/antxhome.cfm
- Safeguard large inventories with recording thermometers and alarms

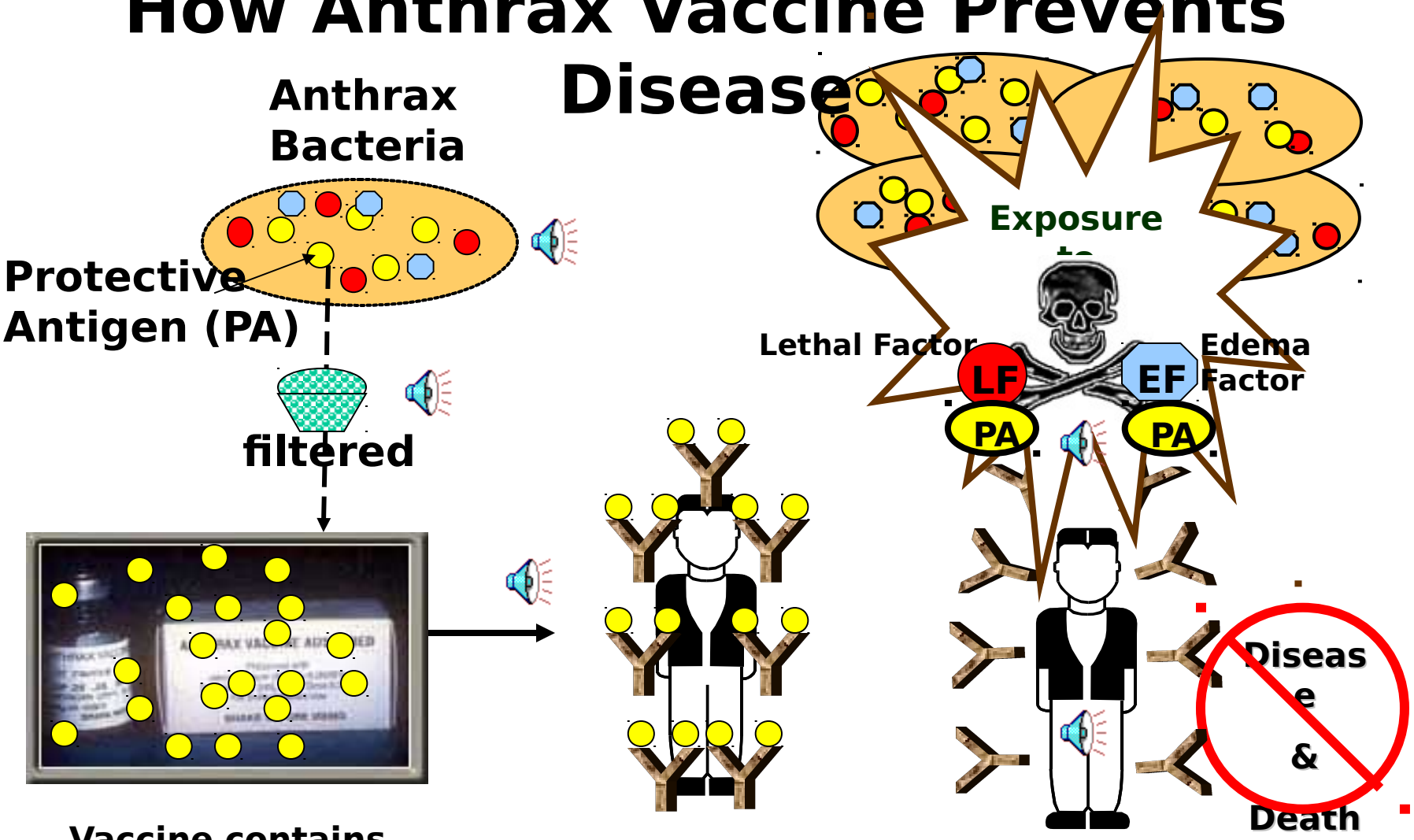
Vaccine Efficacy in Humans

- Brachman et al. *Am J Public Health* 1962;52:432-45
  - Efficacy: 92.5% (95% CI: 65-100%), jointly against cutaneous and inhalation anthrax (table 8)
  - Inhalation anthrax:
    - 5 cases / 448 unvaccinated people
    - 0 cases / 149 vaccinated people
  - Manufacturing improvements, 1960s CDC study
    - Microaerophilic, more PA, less EF and LF
  - Safety and efficacy reaffirmed by FDA advisory panel, *Federal Register* 1985; 50:51002-117
  - Repeated in Final Order issued by FDA, 19 Dec 05

Inhalation Anthrax: Vaccine Efficacy in Non-Human Primates

- 55 monkeys vaccinated twice
  - Challenged with spore aerosol, dozens to thousands of times the median lethal dose, 8, 16, 38, or 100 wks later
  - 52 survived. All unvaccinated control monkeys died
- 10 monkeys vaccinated once
  - Challenged with virulent spores 6 weeks later
  - All survived. All unvaccinated control monkeys died
- Overall, 62 of 65 survived, 95% vaccine protective efficacy against inhaled anthrax spore challenge
- Correlates of immunity to infer from animal to humans have not been fully developed

How Anthrax Vaccine Prevents Disease



Vaccine contains PA, extracted from weakened nonlethal anthrax bacteria.

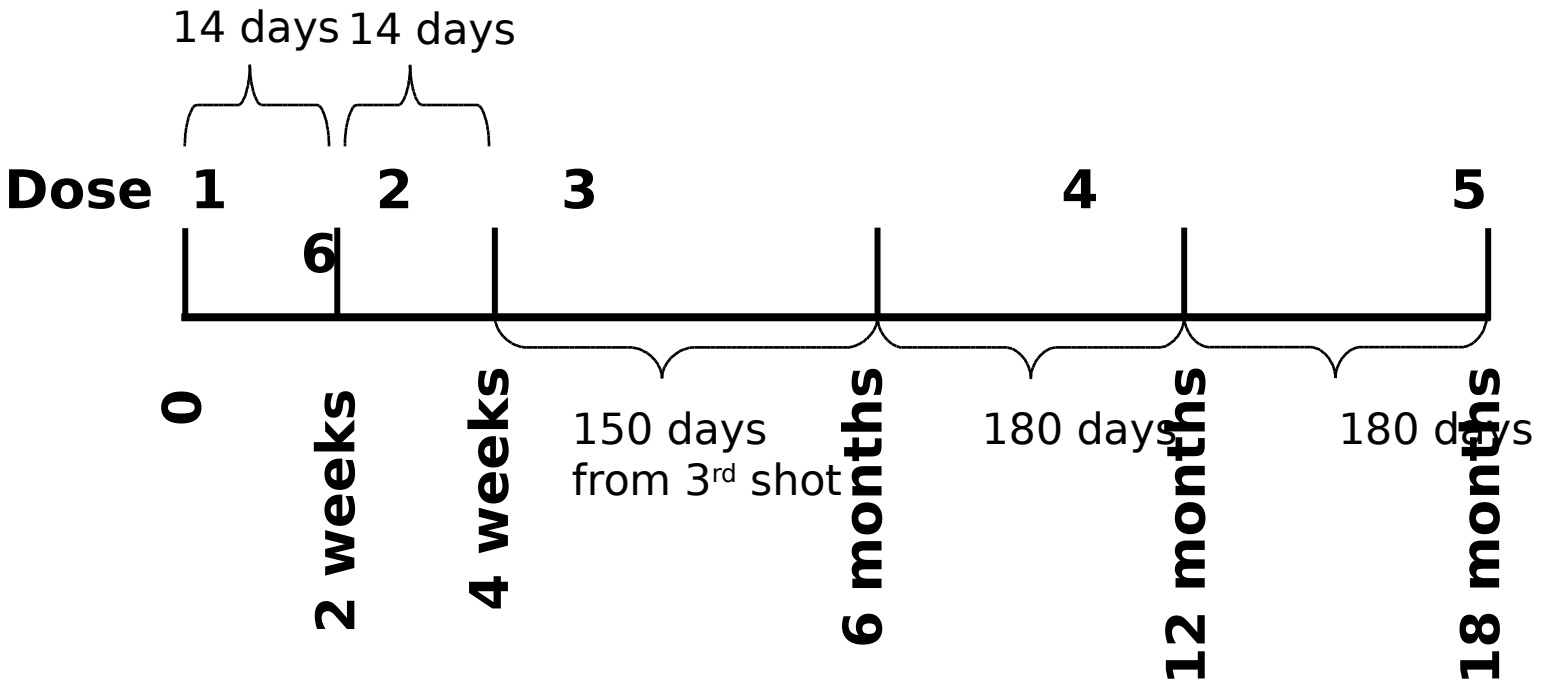
Immune system develops antibodies (Y) to PA, protection from disease.

Antibodies “neutralize” PA, common part of anthrax toxins.

Vaccine Protection Against Different Strains

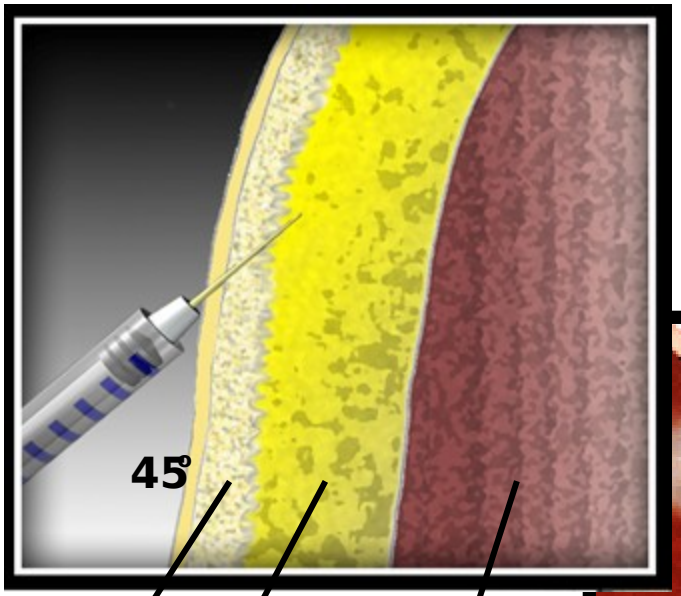
- Vaccine efficacy demonstrated against numerous anthrax strains (types) in various animal studies
- Protective antigen (PA) is the common disease-causing protein in all anthrax strains
- Blocking PA blocks the disease
- America's best scientists, serving on a committee of the National Academy of Sciences, said that anthrax vaccine is an effective vaccine for the protection of humans against ALL forms of anthrax.

Vaccine Schedule



- **Six shots over 18 months, plus annual boosters**
- **Do not compress the schedule**
- **Adjust schedule for individual delays**

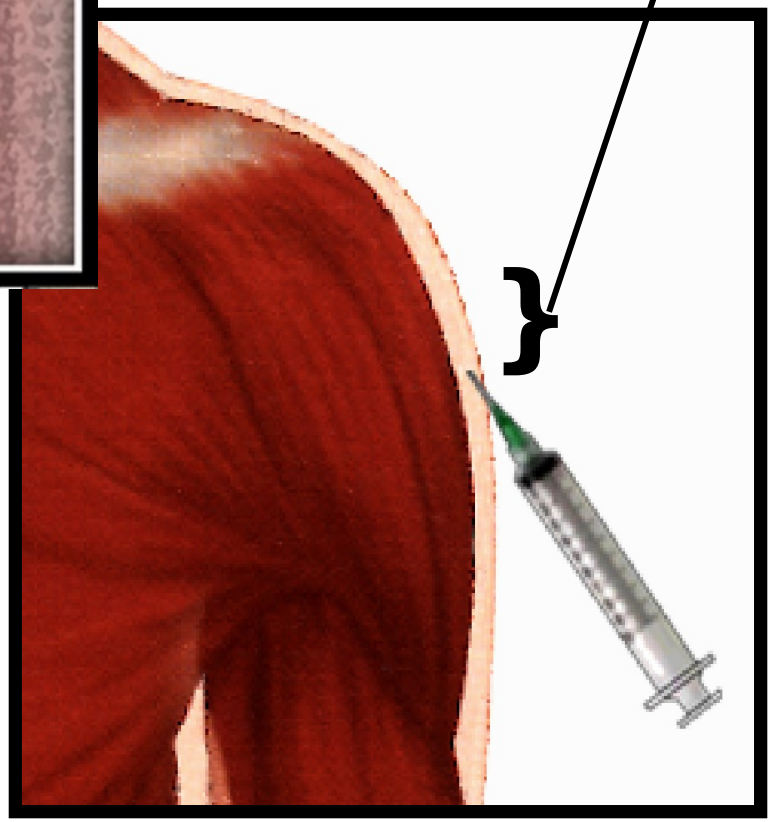
Injection Technique



Skin

Subcutaneous Tissue

Muscle



Deltoid Area

Injection over deltoid rather than triceps is preferred, in case of swelling

Pregnancy

- Vaccinations routinely deferred during pregnancy
- Before vaccination, ask each woman when her last menses was. Was it normal and on time? Postpone, if pregnancy possible.
- No reason to delay conception after vaccination:
  - Anthrax-vaccinated & -unvaccinated women at Fort Stewart (*JAMA*, 2002): same rates of conception, delivery
  - Anthrax-vaccinated & -unvaccinated men at fertility clinic: same sperm concentration, rate of pregnancy
- Vaccination during pregnancy: Preliminary results suggest anthrax vaccine may be linked with an increase in birth defects if given during pregnancy. Do not vaccinate pregnant women unless potential benefits of vaccination outweigh potential risk to fetus.
- **Encourage pregnancy testing.**

Exemptions from Vaccination

- **Some people should not get anthrax vaccine.**
- **Temporary medical exemptions include:**
  - Women who are pregnant, or uncertain if pregnant
  - Acute diseases, surgery
  - Short-term immune suppression
  - Medical evaluation or condition pending
- **Permanent exemptions can include:**
  - Severe allergic reaction or other serious reaction after a previous dose of anthrax vaccine
  - People with a possible history of latex sensitivity
  - HIV infection or other chronic immune deficiencies
  - People who had Guillain-Barré syndrome (GBS)
  - Recovery from previous anthrax infection

Injection-Site Reactions After Anthrax Vaccination

- For both genders, most injection-site reactions last 1 to 3 days and go away on their own
- From Hawaii, Korea, Ft. Bragg, Ft. Detrick, 1993-2000: Redness, itching, swelling (lasting a few days)
  - Less than 1 inch: men up to 30%, women up to 60%
  - 1 to 5 inches: 1% to 5%
  - Greater than 5 inches: 1%
  - Swelling may extend below elbow
  - Soreness or local pain in 8% to 19%
  - Lump: 30% to 90% (may persist a few weeks)

Systemic Events
(Events Beyond Injection Site)

- From 5% to 35% will notice:
  - Muscle or joint aches, headaches, rashes, chills, mild fever, fatigue, swelling extending below elbow, related symptoms
  - Women experience these symptoms more often than men
  - These symptoms usually go away in a few days, less than a week
- Acute allergic reactions occur after any vaccine, about once per 100,000 doses
- The risk of any vaccine causing serious harm, or death, is very small

Managing Adverse Events After Any Vaccination

- Screen for previous adverse reactions
- Do not give next dose, if side effects persist from previous vaccination
- Issue temporary exemption if symptoms persist
- Treat (and pre-treat) adverse events

  See clinical guidelines for managing adverse events after vaccination at www.vhcinfo.org
- Consult provider skilled in diagnosis and management of vaccine adverse events for permanent exemption

Long-Term Studies

Anthrax-Vaccine Recipients Followed 1 Year or Longer

- TAMC-600 Survey (Tripler Army Medical Center)
- Defense Medical Surveillance System (inpatient and outpatient visit surveillance)
- Naval Health Research Center (inpatient and outpatient visit surveillance)
- Army Disability Discharge Database
- CDC dose-reduction / route-change study (placebo control)
- Optic Neuritis Study

Anthrax-Vaccine Recipients Followed for Decades

- Fort Detrick Multi-Dose, Multi-Vaccine Safety Studies (1940s to 1970s)
- Fort Detrick Special Immunization Program (1970s to present)

Adverse Event Reporting

- **Vaccine Adverse Event Reporting System (VAERS):**
  - FDA and CDC review 100% of adverse-event reports
  - All VAERS forms reviewed by independent panel of expert civilian physicians for 4 years
- **DoD <u>requires</u> healthcare workers submit a VAERS Form for:**
  - Loss of duty 24 hours or longer (≥ 1 duty day)
  - Hospitalization
  - Suspected vaccine vial contamination
- **Other submissions are <u>encouraged</u>.**
- **<u>Anyone</u> can submit a VAERS Form !**
- **VAERS Forms may be obtained from:**
  - Your clinic, 1-800-822-7967, or www.vaers.hhs.gov

Reserve Component Adverse-Event Guidance

- **Someone with an adverse event in a non-duty status possibly associated to any vaccination:**
  - Seek medical evaluation at a DoD, USCG, or civilian medical treatment facility, if necessary
  - Report the event to your unit commander or designated representative as soon as possible
  - See local medical department or squadron for guidance
- **Commander will determine Line of Duty and/or Notice of Eligibility status, if required**

Record Keeping

- **Automated immunization tracking (primary)**
  - Service systems and DEERS central repository
- **Written entries:**
  - Health record
  - Deployable Medical Record; Adult Preventive & Chronic Care Flowsheet (DD Form 2766, DD Form 2766C)
  - Yellow Shot Card (PHS-731) (if provided)
- **Required documentation:**
  - Date immunized, name of vaccine, manufacturer, lot number, series number, dosage, provider name and MTF address

What Troops Deserve From Their Health-Care Providers

- **Care, concern, and support**
  - Q&A page at www.anthrax.mil explains many things your patients might ask about
- Quality health care, quality vaccine delivery
- Effective solutions to health-care needs
- Open communication and advice
- Compassion in dealing with adverse events
- Assistance in treating and reporting adverse events

Conclusions

- **Anthrax spores are a lethal threat to our forces.**
- **America's best scientists say the anthrax vaccine is safe and effective, repeatedly.**
- **The life-saving benefits of anthrax vaccine make this an essential immunization program.**
- **For Servicemembers to understand the value of anthrax vaccination, they need your help.**
- **Make sure Servicemembers understand the anthrax vaccine dosing schedule – assist in reminding them when their next vaccination in the series is due.**
- **Expeditiously assist anyone experiencing an adverse event to get proper medical care and advice.**

For More Information

Military Vaccine (MILVAX) Agency

- Website: www.anthrax.mil www.vaccines.mil
- E-Mail: vaccines@amedd.army.mil Toll-Free: 877.GET.VACC

DoD Vaccine Clinical Call Center (24/7): 866.210.6469

For clinical consultation or exemption assistance,

- Website: www.vhcinfo.org E-Mail: askVHC@amedd.army.mil
- Phone: 202.782.0411

CDC National Immunization Hotline: 800.232.2522, www.bt.cdc.gov

To Civilian Healthcare Providers: If military member presents at your office for a condition that may be adverse event caused by military vaccination, please provide appropriate care. For authorization and payment contact **Military Treatment Facility (MTF)** where member is enrolled, OR contact **Military Medical**